

WHAT IS CLAIMED IS:

1 1. A method for producing a non-human animal model of a human or non-human
2 animal disease which comprises transferring at least one aberrant form of at least one
3 gene known to be associated with said disease in humans or non-human animals into
4 appropriate tissue of a living non-human animal under conditions which result in the
5 expression of said at least one aberrant gene, wherein said transferring does not require
6 the modification of the germ-line of said living animal.

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1 2. The method according to claim 1 wherein said human or non-human animal
2 disease is a neurodegenerative disease.

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1 3. The method according to claim 2 wherein said human disease is selected from the
2 group consisting of Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease.

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1 4. The method according to claim 3 wherein said at least one gene is an aberrant
2 form of tau.

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1 5. The method according to claim 3 wherein said aberrant form of tau is P301L,
2 associated with "fronto-temporal dementia with Parkinson's linked to chromosome 17
3 (FTDP-17)".

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1 6. The method according to claim 3 wherein said at least one gene is an aberrant
2 form of alpha-synuclein.

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1 7. The method according to claim 6 wherein said aberrant form of alpha-synuclein is
2 mutant α -synuclein (A30P), associated with Parkinson's Disease.

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1 8. The method according to claim 3 wherein said at least one gene is a mutant
2 amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or combinations thereof,
3 associated with Alzheimer's Disease.

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1 9. The method according to claim 1 which comprises identifying a combination of
2 genes relevant to a particular human pathology and somatically transferring combinations
3 of said genes into tissues appropriate to said particular human pathology in a non-human
4 animal model appropriate to said human pathology.

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1 10. The method according to claim 1 comprising:

- 2 (a) controlling the location to which the genes are transferred, that is spatially
3 controlling gene expression of the transferred genes, in the non-human animal
4 model to which said at least one gene is transferred;
- 5 (b) controlling the temporal effects of transferred genes at specific times in the
6 development of otherwise normal organisms, or in the development of organisms
7 in which germline modifications have previously been made, by selecting the time
8 at which said transferred genes are introduced into said organism, or by
9 controlling the time of expression of said transferred genes;
- 10 (c) evaluating the effects of expression of combinations of multiple transgenes, which
11 in a germline transgenic non-human animal would be difficult if not impossible to
12 achieve due to diseases which might prevent the animal model from maturing to
13 the age-appropriate state for modeling onset of a particular, complex human
14 disease;
- 15 (d) increasing the rate for analyzing multiple genes which contribute to complex,
16 multifactorial human diseases by transferring more than a single gene into an
17 appropriate non-human animal model for said disease;
- 18 (e) testing pharmaceutical agents for their ability to ameliorate specific diseases
19 induced in said non-human animal model;
- 20 (f) studying specific human pathologies induced in said non-human animal model by
21 inducing said pathology in said animal model by transferring said at least one
22 gene into said animal model;
- 23 (g) supplementing an existing germline transgenic model with additional somatically
24 provided gene products to modulate the transgenic model;
- 25 (h) creating a disease condition in an otherwise healthy animal; and
- 26 (i) combinations of (a) –(h).

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1 11. A non-human animal produced by the method of claim 1.

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1 12. A pharmaceutical identified through testing of pharmaceutical compounds
2 using the non-human animal produced according to claim 11.

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1 13. A method for inducing neurofibrillary tangles in the brain of a non-human
2 animal which comprises injecting into the brain of said animal an effective amount of
3 a gene expression construct encoding tau, alpha-synuclein, presenilin-1, amyloid
4 precursor protein, IL6, or a combination thereof.

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1 14. A non-human animal produced according to the method of claim 13.

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1 15. A method for inducing behavioral changes in a non-human animal model
2 which comprises somatic administration of at least one gene directly to the brain of
3 said non-human animal, wherein said at least one gene is associated with a human
4 neurodegenerative disease.

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1 16. The method according to claim 1 wherein said at least one aberrant form
2 of said at least one gene is transferred by means of an adeno-associated virus.

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1 17. A composition comprising at least one gene construct adapted for
2 producing a non-human animal model of a human or non-human-animal disease by
3 transferring at least one aberrant form of at least one gene known to be associated
4 with said disease in humans or non-human animals into appropriate tissue of a living
5 non-human animal under conditions which result in the expression of said at least one
6 aberrant gene, wherein said transferring does not require the modification of the
7 germ-line of said living animal, said composition comprising said at least one
8 aberrant gene in a vector construct which results in active expression of said gene
9 upon introduction into said tissue.

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18. The composition according to claim 17 wherein said at least one gene is an aberrant form of tau.

19. The composition according to claim 18 wherein said aberrant form of tau is P301L, associated with “fronto-temporal dementia with Parkinson’s linked to chromosome 17 (FTDP-17)”.

20. The composition according to claim 17 wherein said at least one gene is an aberrant form of alpha-synuclein.

21. . The composition according to claim 20 wherein said aberrant form of alpha-synuclein is mutant α -synuclein (A30P), associated with Parkinson's Disease.

22. . The composition according to claim 17 wherein said at least one gene is a mutant amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or combinations thereof, associated with Alzheimer's Disease.